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EXAMINER

WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/554,414

Applicant(s)

SZYF ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 August 2005.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-34 and 41-43 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 32-34 and 41-43 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: allowable subject matter.

Response to the Office Action filed on August 30 is acknowledged. Claims 1-31, 37, 38 and 35-40 have been previously cancelled. Claim 44 has been cancelled by the current amendment. Claim 32 has been amended by the current amendment; Claims 32-34 and 41-43 are pending and under examination.

DETAILED ACTION

1. Objections

The objection to the specification and claims are withdrawn in the light of Applicants comments and because claim 32 has been amended.

2. Rejections

2.1. 35 USC, section 112, second paragraph

Claims 32 –34 and 41-44 were rejected in the Office Action of March 31, 2005 (previous action). Rejection of claim 44 is moot because the claim has been canceled. Rejection of claim 32-34 and 41-43 is withdrawn, because claim 32 has been amended.

Rejection caused by amendment

Claim 32 and dependent claims 33-34, 41-43 are rejected under this paragraph, because claim 32 recites the phrase “in a cell comprising amino acids 150-411 of SEQ ID NO: 2” which is confusing. It is DNA demethylase that comprises amino acids 150-411 of SEQ ID NO: 2 and not the cell.

In addition, claim 42 is rejected for lack of antecedent of the phrase “wherein said antagonist is an antisense oligonucleotides of DNA demethylase.” The inhibitor, which

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is an antisense oligonucleotides of DNA demethylase has been canceled from the base claim 32.

2.2. 35 USC, section 112, first paragraph

2.2.1. Lack of written description

Claim 32, 42 and 44 were rejected under 35 U.S.C. 112, first paragraph in the previous action. Rejection of claim 44 is moot because the claim has been canceled. Rejection of claim 32 for the reasons explained in the previous action is withdrawn because the claim has been amended.

Claim 42 was rejected as directed to the subject matter, which is not sufficiently described in the specification, because the specification does not teach that the antisense DNA inhibits the demethylating activity of DNA demethylase.

Response to Applicants' traverse

In their Remarks, page 5, line 13, Applicants write, "Applicants respectfully disagree [to the rejection] as Figure 15 illustrates data using antisense DNA. Furthermore, the experiment and results presented in Figure 15 are discussed in detail on page 43, lines 3 and 17. It is demonstrated that in the application that [sic!] the antisense oligonucleotides (from an expression vector expressing the demethylase cDNA in the antisense orientation) reduces the levels of demethylase protein in the cell thus reducing the availability of demethylation activity. It is also

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demonstrated that reducing demethylase protein leads to inhibition of cell growth on soft agar.”

Applicants' arguments have been fully considered, however neither Fig. 15, nor the text on page 43 demonstrate a reduction in the level of demethylase protein.

The results of Fig. 15, are indirect evidence of the decrease in activity of DNA demethylase in the transfected human cells *in vitro*, because one skilled in the art recognizes that expression of DNA demethylase is, by definition, inhibited by the action of DNA demethylase antisense polynucleotide. In the light of these facts the rejection of claim 42 under 35 USC section 112, first paragraph, made for reasons explained in the previous action is withdrawn.

Rejection caused by the current amendment

Claim 32-34 and 41-43 are rejected as directed to a method of altering activity of DNA demethylase in a cell comprising amino acids 150-411 of SEQ ID NO:2. The claims are generic, because of the broad scope of the phrase “a cell comprising amino acids 150-411 of SEQ ID NO:2”. The claimed genus encompasses methods applicable to any human cell that has active (expressed) DNA demethylase including any cells from the tissue which expresses demethylase, to any cell that was transfected with DNA encoding amino acid 150-411 of SEQ ID NO: 2, and to a cell from any organism transformed with DNA encoding amino acid 150-411 of SEQ ID NO: 2. Applicants teach only one representative genus of methods, i.e., a method directed to inhibition of DNA demethylase in human cells *in vitro*. This description is not sufficient for the

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whole genus of methods claimed by Applicants. Particularly, the specification does not teach how to inhibit DNA demethylase in cells of a whole organism expressing demethylase naturally or transfected to express it. Because of lack of written description of the cells comprising amino acids 150-411 that can be used in the claimed method, one skilled in the art is not convinced that Applicants possessed the claimed invention at the time the application was filed.

2.2.2. Scope of enablement

The current amendment necessitates also rejection for scope of enablement. Claims 32-34 and 41-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of activity of DNA demethylase comprising amino acids 150-411 of SEQ ID NO:2 in human cells (HEK 293) in vitro, does not reasonably provide enablement for inhibiting demethylase in any cell that has, by nature, active (expressed) DNA demethylase including any cell in a tissue which expresses demethylase. The specification is also not enabling for inhibition of the enzyme a cell in any organism transformed with DNA encoding amino acid 150-411 of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered

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in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses a method of inhibiting DNA demethylase in any *in vitro* or *in vivo* cell, wherein the cell expresses amino acids 150-411 of SEQ ID NO:2.

While methods of inhibition of enzymes in cells cultivated *in vitro* are well known in the relevant art, and skills of the artisans highly developed, no one is able to use a method of inhibiting DNA demethylase in a cell in organism without further teachings on the part of Applicants regarding the route of delivering the inhibitor, its doses and schedule of administration. These teachings are missing in the specification. Thus, one skilled in the art is forced to undue experimentation with a low probability of success in making and using the claimed method. Providing teachings regarding inhibition of growth of human HEK293 does not enable a skilled artisan to inhibit DNA demethylase in any cell, particularly a cell in an organism, absent teaching of pharmacokinetics of the recited inhibitors, their doses and schedule of administration. Without a further guidance on the part of Applicants regarding the latter, experimentation left to those in the art is improperly extensive and undue.

3. Conclusion

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The pending claims are rejected. Applicants are remained about allowable subject matter. The claims are directed to the method of use of human DNA demethylase comprising amino acids 150-411 of SEQ ID NO: 2. Applicants are the first to discover human DNA demethylase consisting of amino acid residues 150-411 of SEQ ID NO: 2 and its encoding DNA. The enzyme has a crucial role in regulation of gene expression in human cells, and therefore a great potential pharmaceutical applicability.

The sequence of residues 150-411 of SEQ ID NO: 2 was disclosed first in the Canadian Patent 2,230,991 issued on the application filed May 11, 1998. The PCT application PCT/CA98/01059, of which the instant application is the national stage, was filed November 23, 1998. The disclosure of DNA encoding SEQ ID NO: 2 by Heinrich et al., referred to in the first Office action on merits, mailed May 20, 2003, was later then the disclosure of amino acid residues 150-411 of SEQ ID NO: 2 by Applicants.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

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Patent Examiner


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